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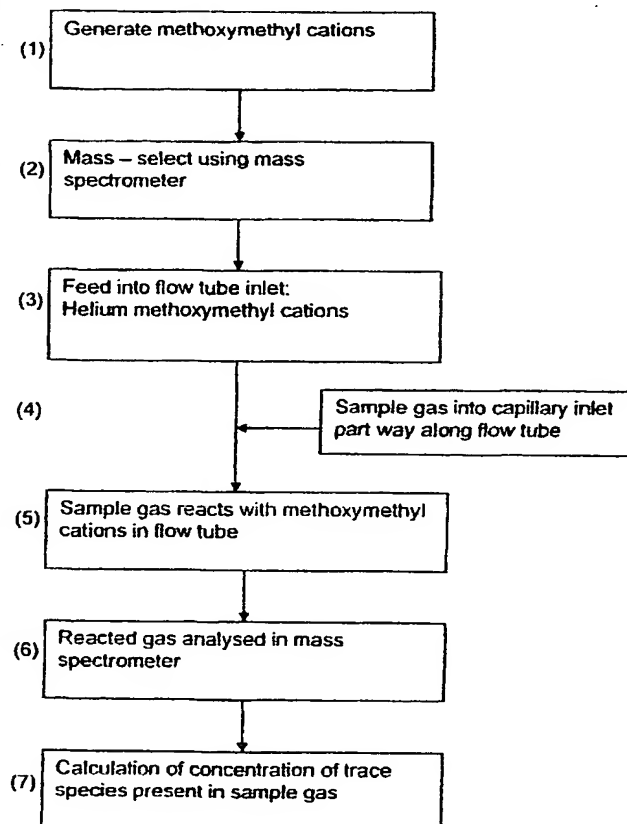
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[Continued on next page]

(54) Title: **IMPROVED METHOD OF CHEMICAL IONIZATION MASS SPECTROMETRY**



(57) Abstract: A method of detecting a substance present in a gas or a gas mixture using SIFT-MS technology comprising the steps of inducing a supply of alkoxymethyl cations into the inlet of the flow tube, reacting a sample of the gas with the alkoxymethyl cations, analysing the reacted gas sample, and calculating the concentration of trace levels of molecules containing heteroatoms in the reacted gas sample.



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ning of each regular issue of the PCT Gazette.*

Title: Improved method of chemical ionization mass spectrometry

## TECHNICAL FIELD

5           The present invention relates to a method for detecting any of a number of substances present in gases or gas mixtures containing alkanes, ethane or ethyne, using chemical ionization mass spectrometry.

## BACKGROUND ART

10           Chemical ionization mass spectrometry has been used for analyte identification since the development of mass spectrometry [Munson, M.S.B.; Fjeld, F.H. *J. Amer. Chem. Soc.*, 88, 2621 -2630 (1966); Munson, M.S.B.; Field, F.H. *J. Amer. Chem. Soc.*, 88, 337 - 4345, (1966); Munson, M.S.B.; Field, F.H. *J. Amer. Chem. Soc.*, 89, 1047-1052, (1967)]. In recent years instruments utilizing chemical ionization sources have  
15           been marketed for analysis of gas mixtures [Linforth, R.; Preece, S. *Technical Note 236*, Micromass Ltd, (1998); Adechy, M.; Shress, V.; Squibb, A. *Peak*, 1,2-4, (2000)]. The combination of a chemical ionization source with flow tube reactor techniques allows both identification and quantification of trace species without internal calibration. Two closely related systems have been developed using this combination of techniques;  
20           *Proton Transfer Mass Spectrometry* [Lindinger, W.; Hansel, A.; Jordan, A. *Int. J. Mass Spectrom; Ion Proc.*, 173, 191-241, (1998)] and *Selected Ion Flow Tube Mass Spectrometry* [Spanel, P.; Smith, D. *Mea. Bioi. Eng. Comput.*, 34, 409-419, (1996)].

25           The selection of the chemical ionizing agent *or* precursor ion is critical to the application of the technique. The precursor ion must be reactive with the analyte molecule(s) but unreactive with the bulk gas within which the analyte is present as a trace component. In most applications to date the bulk gas is ambient air or exhaled breath and the analyte species are various Volatile Organic Compounds (VOCs).

30           Precursor ions which have been in common use include  $\text{NO}^+$ ,  $\text{O}_2^+$ ,  $\text{NH}_4^+$  and  $\text{OH}^-$ . A further important criterion for selection of a chemical ionization precursor is the

facility with which it can be generated in large amounts using typical instrumentation such as an electron impact or microwave discharge source.

It is known from previous experimental work (Freitas, M. A., O'Hair, R. A. J., Int. J. Mass Spectrom; Ion Proc 1998,175, 102-122) that the methoxymethyl cation is not reactive with alkanes but will react with molecules containing heteroatoms. However, the use of  $\text{CH}_3\text{OCH}_2^+$  as a chemical ionization reagent for quantification and identification of analytes has not been tried previously.

#### 10 DISCLOSURE OF INVENTION

In one form the invention is a method of detecting and quantifying trace levels of molecules containing one or more of a range of reactive species, in gases or gas mixtures consisting of alkanes, ethene, or ethyne, said method including using an alkoxyalkyl cation as the chemical ionisation precursor in a selected ion flow tube mass spectrometer.

15 Preferably the method further includes reacting the sample gas to be analysed with the alkoxyalkyl cation in a stream of helium in the flow tube.

Preferably the alkoxyalkyl cation is a methoxymethyl cation.

20 The invention in another aspect comprises a method of detecting and quantifying a gas sample containing trace levels of molecules containing one or more of a range of reactive species, in gases or gas mixtures consisting of alkanes, ethene, or ethyne in a selected ion flow tube mass spectrometer comprising the steps of:

25 producing a supply of alkyoxymethyl cations,  
mass electing the alkyoxymethyl cations,  
inducing a flow of the alkyoxymethyl cations into the inlet of a flow tube of the spectrometer in a carrier flow of helium  
reacting the gas sample with the alkyoxymethyl cations,  
30 analysing the reacted gas sample in the mass spectrometer, and

calculating the concentration of the trace levels of molecules containing heteroatoms present in the reacted gas sample.

Preferably the alkyoxymethyl cation is a methoxymethyl cation.

5

Preferably the range of reactive species includes molecules that contain sulphur, nitrogen, oxygen, phosphorus or silicon heteroatoms,

### **BRIEF DESCRIPTION OF DRAWINGS**

10 By way of example only, a preferred embodiment of the present invention is described in detail with reference to the accompanying flow chart.

### **BEST MODE OF CARRYING OUT THE INVENTION**

Referring to the flow chart, in step 1, a supply of methoxymethyl cations is  
15 produced. This may be done by any of a number of known methods, for example, using the helium flowing afterglow method in which a stream of helium gas is passed in a pyrex or quartz tube through a microwave discharge and a small amount of dimethoxymethane is added to the gas stream emerging from the tube. Methoxymethyl cations are produced by a reaction between the helium metastable species and the  
20 dimethoxymethane.

Another process which may be used to produce the methoxymethyl cations is electron impact using an incandescent rhenium filament within a vacuum chamber filled with a low pressure dimethoxymethane.

25

In step 2, the methoxymethyl cations are mass selected, using a mass spectrometer.

In step 3, the methoxymethyl cations are introduced into the inlet of a flow tube  
30 in a carrier flow of helium, at ambient temperature and at a pressure of about 0.5 Torr.

As the mixture of helium and methoxymethyl cations flow along the flow tube, the sample gas to be analysed is introduced into the flow tube via a capillary inlet (step 4).

5 In step 5, the methoxymethyl cations react with the gas sample, which is primarily one or more alkane gases, but which also contains traces of molecules containing heteroatoms, (e.g. sulphur, nitrogen). This type of gas sample is typical of the type of sample from a leaking gas pipe.

10 The methoxymethyl  $[\text{CH}_3\text{OCH}_2]^+$  ion is unreactive with alkanes, ethene and ethyne, i.e. the hydrocarbons that are present as bulk constituents of natural gas and other hydrocarbon fuel mixtures viz methane,  $\text{CH}_4$ ; ethane,  $\text{C}_2\text{H}_6$ ; propane,  $\text{C}_3\text{H}_8$ ; butane,  $\text{C}_4\text{H}_{10}$ ; ethylene,  $\text{C}_2\text{H}_4$  and acetylene,  $\text{C}_2\text{H}_2$ . The  $\text{CH}_3\text{OCH}_2$  ion is, however, reactive with many sulfur-containing and nitrogen-containing species, including methanethiol,  $\text{CH}_3\text{SH}$ ;  
15 ethanethiol,  $\text{C}_2\text{H}_5\text{SH}$ ; dimethylsulfide,  $(\text{CH}_3)_2\text{S}$  and diethylsulfide,  $(\text{C}_2\text{H}_5)_2\text{S}$ .

The reactivity of  $\text{CH}_3\text{OCH}_2^+$  with selected neutral species in a pressure of 0.5 Torr of helium at room temperature is shown in Table 1.

20 **Table 1**

Neutral	Products	Branching Ratio	Reaction Rate $10^{-9} \text{ cm}^3 \text{ s}^{-1}$
$\text{O}_2$	No reaction		<0.0005
$\text{N}_2$	No reaction		<0.0005
$\text{H}_2\text{O}$	No reaction		<0.0005
$\text{CO}$	No reaction		<0.0005
$\text{CO}_2$	No reaction		<0.0005
$\text{Ar}$	No reaction		<0.0005
$\text{CH}_4$	No reaction		<0.0005
$\text{C}_2\text{H}_6$	No reaction		<0.0005

$C_3H_6$	No reaction		<0.0005
$C_3H_8$	No reaction		<0.0005
$C_4H_{10}$	No reaction		<0.0005
$C_2H_2$	No reaction		<0.0005
$C_2H_4$	No reaction		<0.0005
$CH_3SH$	$CH_3OCH_2 \cdot CH_3SH^+$ $CH_3SHCH^+ + CH_3OH$	(0.95)	0.31
$C_2H_5SH$	$CH_3OCH_2 \cdot C_2H_5SH$ $C_2H_5SHCH^+ + HCHO$	(0.15) (0.85)	0.90
$(CH_2)_2S$	$CH_3OCH_2 \cdot (CH_2)_2S^+$ $(CH_3)_2 \cdot SCH_3^+ +$ $HCHO$	(0.95) (0.05)	1.4
$(C_2H_5)_2S$	$CH_3OCH_2 \cdot (C_2H_5)_2S^+$	(1.0)	1.9

The reacted gas sample produced in step 5 is then analysed in known manner in a mass spectrometer (step 6). Since the methoxymethyl cations react only with the molecules containing the heteroatoms, analysis of the mass spectrometry results can be used to calculate the concentration of the trace species containing heteroatoms present in the alkane gases.

Although the preferred alkoxyalkyl cation is highly preferred, other oxy-radicals can also be employed. For example, but without limiting suitable oxy-radicals are peroxyinitrite, alkoxy cations and reactive oxygen species such as HOCl can be employed with appropriate substrates.

One application of the method herein described is to enable leaks of gas from gas lines or gas containers to be easily and simply detected. Producers of gas often add substances containing sulphur or other odiferous material to gas to aid the detection of leaks, and it is very useful to be able to detect small leaks by detecting the very small quantities of the sulphur-containing or other added material. For this, it is necessary to

have a detection method which reacts with the sulphur-containing or other added material but does not react with the bulk gas or with the major constituents of air,

It will be appreciated that the detection of leaks from has lines is only one of  
5 many applications resulting from the present invention and the method of the present invention has an application in many other fields.

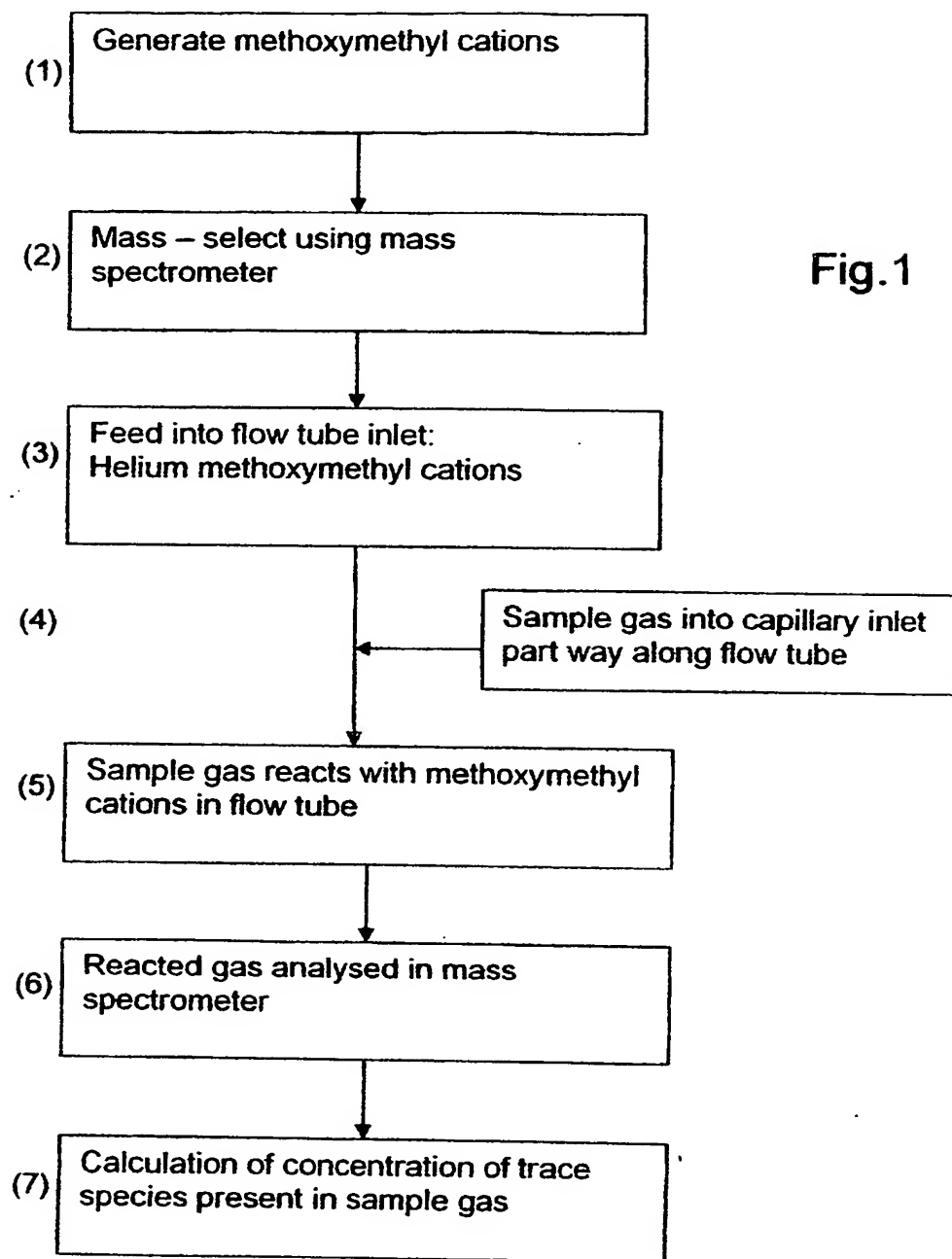
Because the method as herein described uses SIFT-MS technology, it is possible to identify and quantify the reaction product, ethylene, of the methoxymethyl radical  
10 reaction with the substrate. In addition it is possible to carry out the identification and quantification in 'real time' and so can be used to characterise the kinetics of the oxyradical-substrate interaction. Consequently it is possible to make quantitative and kinetic comparisons between different reaction mixtures.

15 Having disclosed preferred forms of the invention, it will be apparent to those skilled in this particular art that modifications and changes can be made to various parameters and yet still come within the general concept of the invention. All such modifications and changes are intended to be included in the scope of the invention.



## CLAIMS

1. A method of detecting and quantifying trace levels of molecules containing one or more of a range of reactive species, in gases or gas mixtures consisting of alkanes, ethene, or ethyne, said method including using an alkoxyalkyl cation as the chemical ionisation precursor in a selected ion flow tube mass spectrometer.  
5
2. The method as claimed in claim 1, further including reacting the sample gas to be analysed with the alkoxyalkyl cation in a stream of helium in the flow tube.
- 10 3. The method as claimed in claim 1, wherein the alkoxyalkyl cation is a methoxymethyl cation.
4. A method of detecting and quantifying a gas sample containing trace levels of molecules containing one or more of a range of reactive species, in gases or gas mixtures consisting of alkanes, ethene, or ethyne in a selected ion flow tube mass spectrometer  
15 comprising the steps of:
  - producing a supply of alkyoxymethyl cations,
  - mass electing the alkyoxymethyl cations,
  - inducing a flow of the alkyoxymethyl cations into the inlet of a flow tube of the  
20 spectrometer in a carrier flow of helium
  - reacting the gas sample with the alkyoxymethyl cations,
  - analysing the reacted gas sample in the mass spectrometer, and
  - calculating the concentration of the trace levels of molecules containing heteroatoms present in the reacted gas sample.
- 25 5. The method as claimed in claim 4, wherein the alkyoxymethyl cation is a methoxymethyl cation.
6. The method as claimed in claim 5, wherein the range of reactive species includes  
30 molecules that contain sulphur, nitrogen, oxygen, phosphorus or silicon heteroatoms,



**A. CLASSIFICATION OF SUBJECT MATTER**Int. Cl. <sup>7</sup>: H01J 49/00, G01N 27/62

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC INT. CL. <sup>7</sup> H01J 49/IC and G01N 27/IC

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Chemical Abstracts

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	<i>J. Am. Soc. Mass Spectrom.</i> (2002), 13, 1028-1033, "Reactions of $\text{CH}_3\text{OCH}_2^+$ with Hydrocarbons and O, N, and S Compounds: Applications for Chemical Ionization in Selected Ion Flow Tube Studies", P. F. Wilson <i>et al.</i> (see entire document)	1-6
Y	Proceedings of the 49 <sup>th</sup> ASMS Conference on Mass Spectrometry and Allied Topics, Chicago, Illinois, May 27-31, 2001, "Like double resonance experiments for studying precursor and intermediate ions involved in ion-molecule reactions produced under self-ionization conditions", M.V. Da Silva, <i>et al.</i> (see entire document, in particular the use of "dimethoxymethane as CI gas reagent" and "a new electrophilic reagent $(\text{CH}_3\text{O})_2\text{CH}^+$ for gas phase cationization")	1-6
Y	<i>Organic Mass Spectrometry</i> (1990), 25, 9-13, "Stereochemical Effects in Mass Spectrometry: Part 8-Chemical Ionization Mass Spectra of Cyclic Glycols and Monosaccharides Using Formaldehyde Dimethyl Acetal as Reagent Gas", Ya-Ping Tu <i>et al.</i> (see entire document)	1-6



Further documents are listed in the continuation of Box C



See patent family annex

* Special categories of cited documents:	
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